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| 10/651,445 | 08/28/2003 | James Gautsch | QBIO1100-7 | 8746 |

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| EXAMINER | |
|---|---|
| OLSON, ERIC | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 06/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/651,445 | GAUTSCH ET AL. | |
| | Examiner | Art Unit | |
| | Eric S. Olson | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *39-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *August 28, 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**Detailed Action**

This application is a divisional application of application 09/510563, filed February 22, 2000, now US patent 6613895, which is a continuation of application 08/591038, filed January 25, 1996, now US patent 6027750, which is a divisional application of application 08/309926, filed September 21, 1994, now abandoned, which is a divisional application of US 07/962418, filed October 16, 1992, now abandoned, which is a continuation in part of US 07/267530, filed November 4, 1988, now abandoned, which is a continuation in part of US 06/903481, filed September 4, 1986, now abandoned. Claims 39-53 are pending in this application and examined on the merits herein. Applicant's preliminary amendment submitted august 28, 2003 is acknowledged wherein claims 1-38 are cancelled and the specification is amended to indicate continuity and further describe the drawings.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 07/267530 and 06/903481, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Therefore the instant application is granted benefit of US application 07/962418, for an effective filing date of October 16, 1992.

**Claim Rejections – 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39-43 and 51-53 are rejected under 35 U.S.C. 102(b) as being anticipated by Mann et al. (reference included with PTO-892) Mann et al. discloses a method of purifying DNA from an agarose gel. (p. 84, right column – p. 85, left column) This method comprises the following steps:

a) Dissolving a slice of DNA-containing agarose in 4M sodium iodide at 65 degrees Celsius. (steps a-b of instant claim 39)

b) Admixing the dissolved agarose sample with insoluble silica matrix (glassmilk).

c) Maintaining the silica in the solution for a time sufficient to bind the DNA and form an insoluble silica-DNA complex (5 min at 0 degrees Celsius).

d) Separating the glass powder from the sample by centrifugation.

e) Eluting the DNA from the glass powder in a TRIS-HCl buffer of pH 7.4

The steps described by Mann et al. are substantially the same as those disclosed in instant claim 39, and are used for the exact same purpose. Although Vogelstein et al.

does not describe the sedimentation time of the silica powder used, it is referred to by the trade name "glassmilk". Melchior, (Message posted may 5, 1992, in an online discussion group at http://www.bio.net/bionet/mm/methods/1992-May/000773.html) discloses a recipe for preparing glassmilk which involves sedimenting silica powder and collecting all silica particles which take longer than 90 minutes to sediment through 800 mL of ddH2O in a 2L flask. Assuming that this quantity of water has a depth of about 10cm, the collected particles have a range of sedimentation times through 100cm of water greater than 15 hours. Thus the glassmilk used by Mann et al. is reasonably expected to have a range of sedimentation times of at least 15 hours, and thus to be a silica matrix comprising at least some particles having the sedimentation characteristics described in instant claims 39-42. Mann et al. teaches a separation step (by centrifugation) according to instant claim 43, a method involving sodium iodide according to instant claim 51 in a concentration of 4M according to instant claim 52, and a method involving a solution containing no cyclohexanediaminetetraacetate according to instant claim 53. Thus every element of instant claims 39-43 and 51-53 is anticipated by Mann et al.

**Claim Rejections – 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 39-48, 49-51, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vogelstein et al. (reference included with PTO-892) in view of Shimizu et al. (US patent 4600507, reference cited in PTO-892), further in view of Ishikawa et al. (US patent 4430213, reference cited in PTO-892) Vogelstein et al. discloses a method for the purification of DNA from an agarose gel. This method is very similar to the method disclosed in the instant claims. In particular, the method of Vogelstein et al. comprises the following steps:

a) Dissolving a slice of DNA-containing agarose in saturated sodium iodide.

b) Admixing the dissolved agarose sample with insoluble glass powder.

c) Maintaining the glass powder in the solution for a time sufficient to bind the DNA and form an insoluble glass-DNA complex.

d) Separating the glass powder from the sample by centrifugation.

e) Eluting the DNA from the glass powder in a TRIS-HCl buffer of pH 7.2

Vogelstein et al. discloses three different types of glass powders with varying sedimentation times. The powder most effective in binding DNA is one which has a sedimentation rate in water of 0.25 cm/min. (p. 616, figure 1, table A) This glass therefore has a sedimentation time of 6h, 40 min through 100cm of water, falling within the limitations of instant claims 39-41. Vogelstein et al. does teach a separation step according to instant claim 43, a method involving sodium iodide according to instant claim 51, and a method involving a solution containing no cyclohexanediamine-tetraacetate according to instant claim 53.

The method disclosed by Vogelstein does not include a step equivalent to step B of instant claim 39 in which the agarose sample is maintained at a temperature of between 45 and 65 Celsius until the entire sample is dissolved. Vogelstein et al. does not disclose a method according to instant claim 39 where the sodium iodide solution is buffered with 0.1-1M tris(hydroxymethyl)aminomethane or phosphate buffer, with a pH value between 7.2-7.8 according to instant claims 49-50. Vogelstein et al. also does not teach a method in which the silica matrix is separated from the sample by filtration, either by vacuum filtration or centrifugal filtration, according to instant claims 44-48, or one involving a glass powder or silica matrix having a sedimentation time of 1-6 weeks as described by instant claim 42.

Ishikawa discloses a filtration apparatus comprising two airtight chambers separated by a filter, having an inlet and outlet as described in instant claim 46. Shimizu et al. discloses a centrifuge tube having a filter membrane arranged such that a liquid sample placed inside the centrifuge tube will pass through the membrane and be filtered upon centrifugation. The bottom of the tube comprises a detachable receptacle for the recovery of filtrate. (Sheet 1 of 3, figure 1, for example)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of Vogelstein et al. by dissolving the agarose sample at an elevated temperature between 45 and 65 degrees Celsius, and to buffer the solution with 0.1-1M tris or phosphate buffer at a pH between 7.2 and 7.8. It would also have been obvious to one of ordinary skill in the art to separate the silica-DNA bound complex from the sample using either pressure filtration with a device such as that

described by Ishikawa or by centrifugal filtration using a device such as that described by Shimizu et al., or an obvious modification thereof, and to utilize in the filtration step a membrane with an appropriate pore size, such as between 0.1 and 1.0 micrometers as recited by instant claim 45. It would also have been obvious to one of ordinary skill in the art to use a glass powder having a sedimentation time through 100 cm of water of 1-6 weeks according to instant claim 42.

One of ordinary skill in the art would have been motivated to increase the temperature of the sample during dissolution of the agarose in order to speed up the dissolution step. One of ordinary skill in the art would have been motivated to buffer the gel-dissolving solution in order to stabilize the DNA in cases in which this solution is left to stand for extended periods of time before the separation step. One of ordinary skill in the art would have been motivated to use one of the filtration devices of Shimizu et al. or Ishikawa to recover the glass-DNA bound complex in better yields than those obtained by simple centrifugation and to avoid loss of glass-DNA complex which would occur when pouring or pipetting the supernatant out of the centrifuge tube after centrifugation. One of ordinary skill in the art would have been motivated to use a glass powder with a slower sedimentation rate in order to increase the binding capacity of the silica matrix.

One of ordinary skill in the art would reasonably have expected success because it is well known that elevated temperatures cause most materials to dissolve faster, and because buffering of DNA solutions at a pH between 7.2 and 7.8 prior to storage is well known in the prior art. For example, Vogelstein et al. discloses that the isolated DNA

samples were ultimately dissolved in a Tris-acetate solution at pH 7.8 for storage after being isolated by the claimed method. The filtration devices of Shimizu et al. and Ishikawa are both described in the literature to be useful for the purpose of separating fine particulate matter from a liquid sample, and thus one of ordinary skill in the art would reasonably expect that they would be useful for separating the glass-DNA matrix from the liquid sample. One of ordinary skill in the art would reasonably have expected success in using more finely ground silica particles because figure 1 of Vogelstein et al. discloses that smaller, slower sedimenting particles have a greater binding capacity for DNA. Although smaller glass particles are more difficult to separate by centrifugation, the use of a filter according to Shimizu et al. or Ishikawa to separate the glass-DNA complex from the sample eliminates the centrifugation step and overcomes this obstacle. It should be noted that the protocol disclosed by Vogelstein et al. is a proof of concept experiment and that any implementation of said protocol as a routine technique for the recovery of DNA would incorporate obvious modifications for the purpose of convenience and optimized yield, such as those mentioned above.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 44-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mann et al. (reference included with PTO-892) in view of Shimizu et al. (US patent 45600507, reference cited in PTO-892), further in view of Ishikawa et al. (US patent 4430213, reference cited in PTO-892) Mann et al. discloses a method of purifying DNA

from an agarose gel. (p. 84, right column – p. 85, left column) This method comprises the following steps:

a) Dissolving a slice of DNA-containing agarose in 4M sodium iodide. (steps a-b of instant claim 39)

b) Admixing the dissolved agarose sample with insoluble silica matrix (glassmilk).

c) Maintaining the silica in the solution for a time sufficient to bind the DNA and form an insoluble silica-DNA complex (5 min at 0 degrees Celsius).

d) Separating the glass powder from the sample by centrifugation.

e) Eluting the DNA from the glass powder in a TRIS-HCl buffer of pH 7.4

The steps described by Mann et al. are substantially the same as those disclosed in instant claim 39, and are used for the exact same purpose. Although Vogelstein et al. does not describe the sedimentation time of the silica powder used, it is referred to by the trade name "glassmilk". Melchior, (Message posted may 5, 1992, in an online discussion group at http://www.bio.net/bionet/mm/methods/1992-May/000773.html, included with PTO-892) discloses a recipe for preparing glassmilk which involves sedimenting silica powder and collecting all the silica particles which take longer than 90 minutes to sediment through 800 mL of ddH2O in a 2L flask. Assuming that this quantity of water in this size flask has a depth of 10cm, the collected particles have a range of sedimentation times through 100cm of water greater than 15 hours. Thus the glassmilk used by Mann et al. is reasonably expected to have a range of sedimentation times greater than about 15 hours, and thus to be a silica matrix comprising at least

some particles having the sedimentation characteristics described in instant claims 39-42. Mann et al. does not teach a method involving recovering the silica-DNA complex by filtration in the manner of instant claims 44-48.

Ishikawa discloses a filtration apparatus comprising two airtight chambers separated by a filter, having an inlet and outlet as described in instant claim 46. Shimizu et al. discloses a centrifuge tube having a filter membrane arranged such that a liquid sample placed inside the centrifuge tube will pass through the membrane and be filtered upon centrifugation. The bottom of the tube comprises a detachable receptacle for the recovery of filtrate. (Sheet 1 of 3, figure 1, for example)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of Mann et al. by separating the silica-DNA bound complex from the sample using either pressure filtration with a device such as that described by Ishikawa or by centrifugal filtration using a device such as that described by Shimizu et al., or an obvious modification thereof, rather than separating the bound complex by centrifugation. It would also have been obvious to one of ordinary skill in the art to utilize in the filtration step a membrane with an appropriate pore size, such as between 0.1 and 1.0 micrometers as recited by instant claim 45.

One of ordinary skill in the art would have been motivated to use one of the filtration devices of Shimizu et al. or Ishikawa to recover the glass-DNA bound complex in better yields than those obtained by simple centrifugation and to avoid loss of glass-DNA complex which would occur when pouring or pipetting the supernatant out of the centrifuge tube after centrifugation.

One of ordinary skill in the art would reasonably have expected success because the filtration devices of Shimizu et al. and Ishikawa are both described in the literature to be useful for the purpose of separating fine particulate matter from a liquid sample.

Thus the invention taken as a whole is *prima facie* obvious.

**Summary**

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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